REMARKS/ARGUMENTS

Reconsideration of this application and entry of the foregoing amendments are respectfully requested.

Claim 11 has been revised to define the invention with additional clarity. The basis for the amendment is found, for example, at page 4, line 4 of the subject specification. Claims 18 and 19 have been cancelled without prejudice. That claims have been revised/cancelled should not be taken as an indication that Applicant agrees with any position taken by the Examiner. Rather, the revisions/cancellations are made merely to advance prosecution and Applicant reserves the right to pursue any deleted subject matter in a continuation application.

Claims 11-19 stand rejected under 35 USC 112, first paragraph, as allegedly being non-enabled. Withdrawal of the rejection is submitted to be in order in view of the above-noted claim revisions and for the reasons that follow.

At the outset, the Examiner's attention is directed to the fact that claim 11 as now presented recites human IL-10, and forms thereof having at least 95% homology with human IL-10 that retain the anti-inflammatory healing functionality of human IL-10. The claim thus allows for up to about 8 of the 160 amino acids of human IL-10 to be altered/deleted.

The Examiner appears to acknowledge (for example, on page 7 of the Action, last paragraph) that the disclosure supports claims reciting human IL-10 and modified forms thereof taught in WO 95/03411. It is submitted that the scope of claim 11 as now

presented is entirely appropriate given the scope of the disclosure as acknowledged by the Examiner.

WO 95/03411 describes a specific human IL-10 sequence (shown in SEQ ID NO:4 of that application) and makes reference to variants (e.g., allelic variants) having one or more conservative amino acid substitutions (page 5, lines 19-24). WO 95/03411 specifically teaches a form of human IL-10 bearing a substitution at position 157. WO 95/03411 also teaches at page 6, first full paragraph, that about the 12 C-terminal residues can be deleted, preferably 8, more preferably 3 or 4 (see SEQ ID NOs:2 and 3). WO 95/03411 further teaches that up to 11 amino acids can be deleted from the N-terminus (see page 6, second paragraph). WO 95/03411 thus teaches a number of species within the claimed genus. In addition, WO 95/03411 discloses methods suitable for production of further fragments and derivatives capable of use in accordance with the invention. Furthermore, since the sequence of the gene encoding IL-10 was known, manufacture of additional derivatives or fragments would have required only the use of standard protocols.

The presence or absence of the functionality required by the claims could be readily assessed using comparative experiments in which the extent of inflammation occurring in wounds treated with the putative agent is compared with inflammation occurring in wounds treated with IL-10. The Examiner's attention has been drawn previously to the following documents which detail suitable models of wound healing:

Shah M., Foreman D.M. and Ferguson, M.W.J.
"Neutralising antibody to TGFβ1,2, reduces scarring in adult rodents".
Journal of Cell Science, 107, 1137-1157, 1994

Shah M., Foreman D.M. and Ferguson, M.W.J.
"Neutralisation of TGFβ1 and TGFβ2 or exogenous addition of TGFβ3 to cutaneous rat wounds reduces scarring".
Journal of Cell Science, 108, 985-1002, 1995.

The foregoing is believed to make clear the adequacy of the disclosure. According, reconsideration is requested.

Claims 11 to 19 stand rejected under 35 USC 112, first paragraph, as allegedly lacking written description. Withdrawal of the rejection is submitted to be in order in view of the above-noted claim amendments and for the reasons that follow.

In maintaining the rejection, the Examiner refers to the claims as genus claims. While that is the case, the claims as now presented define a relatively small genus. As noted above, claim 11 recites human IL-10 and forms thereof having at least 95% homology with human IL-10 and that retain the anti-inflammatory functionality of human IL-10. The claim thus allows for only about 8 of the 160 amino acids of human IL-10 to be altered/deleted. As detailed above, WO 95/03411 teaches a representative number of species within the presently claimed genus. WO 95/03411 teaches a form of IL-10 bearing a substitution at position 157, as well as various C-terminal truncated forms thereof (SEQ ID NOs:2 and 3 being two specific examples). Additionally, WO 95/03411 teaches that up to 11 amino acids can be deleted from the N-terminus.

Given the scope of the claims as now presented, and the clear teaching of a representative number of species within the claimed genus, it will be apparent that Applicant had full possession of the invention at the relevant date and reconsideration is requested.

Claims 11-19 stand rejected under 35 USC 112, first paragraph, as allegedly lacking written description given the use of the phrase "anti-inflammatory healing functionality". The rejection is traversed.

The phrase "anti-inflammatory healing functionality" was introduced to provide further definition to the fragments or partially modified forms of human IL-10 suitable for use in accordance with the invention. Basis for the wording "anti-inflammatory healing functionality" can be found in the final paragraph of page 3 of the specification, where it is stated:

> 'By "fragment or partially modified form thereof" is meant a fragment or partially modified form of IL-10 which retains *the anti-inflammatory healing functionality of IL-10*'.

(Emphasis added).

This paragraph provides clear support for the claim language and reconsideration is requested.

Claims 11-19 stand rejected under 35 USC 112, second paragraph, as allegedly being indefinite. Withdrawal of the rejection is submitted to be in order for the reasons that follow.

Basis for the Examiner's assertion that the phrase "anti-inflammatory healing functionality" is indefinite is not understood. It is believed clear on its face that the forms of IL-10 to which the phrase relates must function, as does IL-10, as an anti-inflammatory agent that promotes healing. The Examiner is respectfully requested to further explain the basis for his concern or withdraw the rejection.

Claims 11-19 stand rejected as allegedly representing obviousness-type double patenting over claims 1-10 of USP 6,387,364. It is again noted that the rejection can be overcome by the filing of a Terminal Disclaimer and the Examiner is again urged to hold the rejection in abeyance until the case is otherwise in condition for allowance.

Claims 11-19 stand rejected under 35 USC 102(b) as allegedly being anticipated by Gordon et al (WO 93/19770). The rejection is again traversed.

The rejection of the claims as anticipated is based on that which the Examiner believes to be inherent in the teachings of Gordon et al. It is now well established that for a rejection based on inherency to be proper, the subject matter claimed must necessarily flow from the teachings of the cited art. Respectfully, that is not the case here.

The claims require administering to a patient an amount of human IL-10, or partially modified form thereof as defined in (ii) of claim 11, sufficient to promote the healing of a wound, or fibrotic disorder, with reduced scarring.

Gordon et al teaches (i) a composition comprising IL-4 and IL-10 for use in treating an acute or chronic inflammation, (ii) a method of treating an acute or chronic inflammation comprising applying IL-4 and IL-10 to the inflammation to promote or

enhance tissue repair, and (iii) a method of promoting healing by applying a mixture of IL-4 and IL-10 to an acute or chronic inflammation to produce macrophages with a healing phenotype (see pages 10 and 11). The *in vivo* examples of Gordon et al involve the use of combinations of IL-4 and IL-10 and wound observation at 72 hours (see, Example 5). Given these teachings, no basis is seen for the Examiner's rejection which, to be proper, requires that the amount of IL-10 administered be such that healing of a wound or fibrotic disorder is promoted with reduced scarring. Nothing in the Examples of Gordon et al nor in the description of the invention inherently teaches administration of an amount of IL-10 sufficient to exert the required effect. Further, the conditions of the working *in vivo* examples (including the brevity of the observation period) are such that reduction in scarring certainly does not necessarily flow.

While the instant claims do not exclude the use of IL-4, they do require that IL-10 be given in an amount sufficient to promote healing with reduced scarring. No basis is found for the Examiner's assertion that "the concentrations of IL-10 used in the method of [Gordon et al] to treat inflammation (i.e. wound) would inherently be the same concentration of IL-10 required to heal wounds with reduced scarring". This is the case at least in part because Gordon et al does not teach the use of IL-10 alone in an amount sufficient to treat inflammation.

In view of the above, reconsideration is requested.

Claims 16 and 17 stand rejected under 35 USC 103 as allegedly being obvious over Gordon et al. The rejection is traversed.

It is now well settled that inherency and obviousness are different questions. "That which may be inherent is not necessarily known. Obviousness cannot be predicated on what is unknown." In re Spormann and Heinke, 150 USPQ 449, 452 (CCPA 1966).

Withdrawal of this rejection is clearly in order.

This application is submitted to be in condition for allowance and a Notice to that effect is requested.

Respectfully submitted,

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